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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Attorney Docket No. MBHB00-327-A)

TECH CENTER 1600/2900

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In Re Application of:)
Bacus et al.) Examiner: Unassigned
Serial No. 09/835,603) Art Unit: 1632
Filed: April 16, 2001) Confirmation number: 3061
For: METHOD FOR QUANTIFICATION OF)
AKT PROTEIN EXPRESSION)

TRANSMITTAL LETTER

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

In regard to the above identified application,

1. We are transmitting herewith the attached:


- ☒ Information Disclosure Statement;
- ☒ Form PTO-1449 including (27 cited references)
- ☒ International Search Report for PCT/US01/12288; and
- ☒ Return Postcard

2. No fees are due at this time.

3. **GENERAL AUTHORIZATION TO CHARGE OR CREDIT FEES:** Please charge any additional fees or credit overpayment to Deposit Account No. 13-2490. A duplicate copy of this sheet is enclosed.

4. **CERTIFICATE OF MAILING UNDER 37 CFR §1.8:** I hereby certify that I directed that the correspondence identified above be deposited with the United States Postal Service as "First Class Mail," addressed to the Commissioner for Patents, Washington, DC 20231 on the date indicated below.

Respectfully submitted,



Andrew W. Williams
Registration No. 48,644

Date: October 30, 2002

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PATENT**UNITED STATES PATENT AND TRADEMARK OFFICE**

(Attorney Docket No. MBHB00-327-A)

In Re Application of:

Bacus et al.Examiner: **Unassigned**Serial No. **09/835,603**Art Unit: **1632**Filed: **April 16, 2001**Confirmation number: **3061**For: **METHOD FOR QUANTIFICATION OF
AKT PROTEIN EXPRESSION****INFORMATION DISCLOSURE STATEMENT**Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Pursuant to 37 C.F.R. §§1.97-1.98, and in accordance with the duty of candor set forth in 37 C.F.R. §1.56, Applicants wish to make the following references of record in the above-identified application. Copies of the references cited below are enclosed along with a copy of completed PTO Form-1449.

Applicants also submit herewith a copy of the International Search Report issued from the European Patent Office for International Application No. PCT/US01/12288.

CITED REFERENCES**I. U.S. PATENT APPLICATION PUBLICATION DOCUMENTS**

Patent Application Publication Number	Publication Date	<u>Applicant</u>
1. 2001/044124	11/22/2001	Bacus
2. 2002/037541	3/28/2002	Obata

CERTIFICATE OF MAILING (37 C.F.R. 1.8)

I hereby certify that this correspondence is being deposited with the United States Postal Service as "First Class Mail," addressed to the Commissioner for Patents, Washington, DC 20231 on the date indicated below.

Date: October 30, 2002

Andrew W. Williams

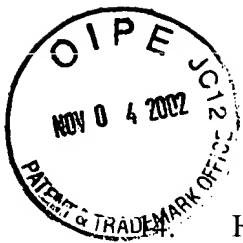


II. FOREIGN PATENT DOCUMENTS

	<u>Document Number</u>	<u>Publication Date</u>	<u>Country/ Patent Office</u>
3.	WO 01/79557	10/25/2001	PCT
4.	WO 01/79855	10/25/2001	PCT

III. OTHER DOCUMENTS

5. Arteaga et al., "p185^{c-erbB-2} Signaling Enhances Cisplatin-induced Cytotoxicity in Human Breast Carcinoma Cells: Association between an Oncogenic Receptor Tyrosine Kinase and Drug-Induced DNA Repair," Cancer Res., 54:3758-3765, 1994.
6. Bacus et al., "AKT2 is frequently upregulated in HER-2/neu-positive breast cancers and may contribute to tumor aggressiveness by enhancing cell survival," Oncogene, England, Vol. 21, No.22:3532-3540, May 16, 2002.
7. Bacus et al., "Akt2 upregulation in HER-2/neu-overexpressing breast cancers: Implications to their clinical and biological behavior," Proceedings of the American Association For Cancer Research Annual, Vol. 42:243, March 2001.
8. Bacus et al., "Neu differentiation factor (Heregulin) activates a p53-dependent pathway in cancer cells," Oncogene, 12:2535-2547, 1996.
9. Bacus et al., "Potential Use of Image Analysis for the Evaluation of Cellular Predicting Factors for Therapeutic Response in Breast Cancers," Anal. Quant. Cytol. Histol., 19:316-328, 1997.
10. Bacus et al., "Type 1 Receptor Tyrosine Kinases Are Differentially Phosphorylated in Mammary Carcinoma and Differentially Associated with Steroid Receptors," American Journal of Pathology, 148(2):549-558, 1996.
11. Cantley and Neel, "New insights into tumor suppression: PTEN suppresses tumor formation by restraining the phosphoinositide 3-kinase/AKT pathway," Proc. Natl. Acad. Sci. U.S.A., 96:4240-45, 1999.
12. Cobleigh et al., "Mutational Study of the Efficacy and Safety of Humanized Anti-HER2 Monoclonal Antibody in Women Who Have HER2-Overexpressing Metastatic Breast Cancer That Has Progressed After Chemotherapy for Metastatic Disease," J. Clin. Oncol., 17:2639-2648, 1999.
13. Datta et al., "Cellular survival: a play in three Akts," Genes and Dev., 13:2905-27, 1999.



- Hancock et al., "A Monoclonal Antibody against the *c-erbB-2* Protein Enhances the Cytotoxicity of *cis*-Diamminedichloroplatinum against Human Breast and Ovarian Tumor Cell Lines," *Cancer Res.*, 51:4575-4580, 1991.
15. Li et al., "PTEN, a Putative Protein Tyrosine Phosphatase Gene Mutated in Human Brain, Breast, and Prostate Cancer," *Science* 275:1943-47, 1997.
 16. Liaw et al., "Germline mutations of the PTEN gene in Cowden disease, an inherited breast and thyroid cancer syndrome," *Nat. Genet.*, 16:64-67, 1997.
 17. Liu et al., "Heregulin Regulation of Akt/Protein Kinase B in Breast Cancer Cells," *Biochem. Biophys. Res. Commun.*, 261:897-903, 1999.
 18. National Institute of Health Consensus Development Conference: Steroid Receptors in Breast Cancer, 1979, Bethesda, MD.
 19. Nelen et al., "Germline mutations in the PTEN/MMAC1 gene in patients with Cowden disease," *Hum. Mol. Genet.*, 6:1383-87, 1997.
 20. Peles et al., "Cell-type specific Interaction of Neu differentiation factor (NDF/hergulin) with Neu/HER-2 suggests complex ligand – receptor relationships," *EMBO J.*, 12(3):961-971, 1993.
 21. Peles et al., "Neu and its Ligands: From an Oncogene to Neural Factors," *BioEssays*, 15(12):815-924, 1993.
 22. Pettmann and Henderson, "Neuronal Cell Death," *Neuron*, 20:633-47, 1998.
 23. Shak, "Overview of the Trastuzumab (Herceptin) Anti-HER2 Monoclonal Antibody Clinical Program in HER2-Overexpressing Metastatic Breast Cancer," *Semin. Oncol.*, 26:71-77, 1999.
 24. Sliwkowski et al., "Nonclinical Studies Addressing the Mechanism of Action of Trastuzumab (Herceptin)," *Semin. Oncol.*, 26:60-70, 1999.
 25. Yang et al., "Bad, a Heterodimeric Partner for Bcl-x_L and Bcl-2, Displaces Bax and Promotes Cell Death," *Cell*, 80:285-91, 1995.
 26. Zundel and Giaccia, "Inhibition of the anti-apoptotic PI(3)K/Akt/Bad pathway by stress," *Genes Dev.*, 12:941-46, 1998.
 27. Daly et al., "Neu differentiation factor induces ErbB2 down-regulation and apoptosis of ErbB2-overexpressing breast tumor cells," *Cancer Res.*, 57(17):3804-11, 1997.



IV. DISCUSSION

Applicants submit that these documents, whether taken alone or in combination, fail to show or suggest the claimed subject matter. Applicants request that the Examiner consider the entirety of each document and make them of record in this application by initialing on Form PTO-1449. Such initialing is requested even if the Examiner does not consider a cited document to be sufficiently pertinent to use in a rejection, or otherwise does not consider it to be prior art for any reason, or even if the Examiner does not believe that Applicants have fully complied with the guidelines for citation. This is requested so that each document becomes listed on the face of the patent issuing on the present application. Applicants' submission of these documents for consideration is not to be construed as an admission that the documents qualify as prior art to the claimed subject matter, a representation that a search has been made, nor as an admission that the information is considered to be material to patentability.

Portions of the references may be material to the examination of the pending claims, although no such admission is intended. 37 C.F.R. §1.97(h). The references have not been reviewed in sufficient detail to make any other representation and, in particular, no representation is intended as to the relative importance of any portion of the references.

Respectfully Submitted,

McDonnell Boehnen Hulbert & Berghoff

Date: October 30, 2002

By:

Andrew W. Williams

Reg. No. 48,644